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Study shows PET can measure effectiveness of novel breast cancer treatment

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A new study published in the July issue of The *Journal of Nuclear Medicine* shows that positron emission tomography (PET) scans in mice can be used to determine whether a novel type of breast cancer treatment is working as intended.

Researchers successfully used PET and a specially-developed radioactive compound to image HER2—a protein often associated with aggressive breast cancer—in breast cancer cells before and after treatment aimed at decreasing HER2 expression. This molecular imaging methodology could facilitate development of new targeted therapies not only for breast cancer, but also for certain types of ovarian, prostate, and lung cancers that may be aggravated due to HER2.

"Obtaining an accurate assessment of the HER2 expression levels in breast cancer tumors is absolutely essential to know whether treatment aimed at reduction of the protein levels in tumor cells is effective," said Jacek Capala, senior author of the study and investigator for the radiation oncology branch of the National Cancer Institute, National Institutes of Health, Bethesda, Md. "Our study indicates that PET could be a powerful tool both to identify patients who might benefit from targeted molecular therapies and to manage their care by measuring response to treatment. As research into HER2 therapies continues, similar techniques could be developed for other cancers overexpressing different proteins."

Much new research has been focused on developing therapies targeted to

HER2. This protein is overexpressed in approximately 20 percent of breast cancers and also in some ovarian, prostate and lung cancers. Tumors that have an overabundance of HER2 protein are more aggressive and more likely to recur than tumors that do not overexpress the protein.

The imaging technique developed in the study represents a breakthrough in measuring HER2 expression. The conventional method requires biopsies of tumors that have been removed from the body; however, these samples may not represent the overall characteristics of the tumor and may not accurately estimate HER2 expression. In addition, there are currently no means to evaluate how long a therapeutic agent takes to affect the targeted tumors and how long the effects last.

In the study, researchers attached the radioactive nuclide flourine-18 to an HER2-binding variant of a small protein known as an Affibody molecule. PET scans can detect the Affibody compound and allow researchers to visualize breast cancer tumors with HER2 protein in mice. These molecules can also be engineered to specifically bind to other targets for cancer diagnosis and therapy.

The researchers implanted human breast cancer cells—expressing either very high or high levels of HER2—under the skin of mice to show that this method of imaging can be used to monitor changes in HER2 expression after treatment. Researchers then intravenously injected the HER2-targeting Affibody compound and performed PET imaging three to five weeks after tumors had formed. Four doses of the drug 17-DMAG were administered, which decreases HER2 expression, spaced 12 hours apart. PET scans were performed before the treatment and after each dose.

The researchers found that HER2 expression was reduced by 71 percent in mice bearing tumors with very high levels of HER2 protein and by 33

percent in mice bearing tumors with high levels of the protein, compared to the levels measured before treatment and to tumors that did not receive the treatment. Researchers confirmed their data using established laboratory techniques to determine the concentrations of HER2 proteins in the same tumors after they were removed from the mice.

Source: Society of Nuclear Medicine (news : web)